Amendment and Response

Serial No.: 10/780,797 Confirmation No.: 1508 Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2, 3-DIOXYGENASE IN COMBINATION WITH OTHER

THERAPEUTIC MODALITIES

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the aboveidentified application:

- 1. (Currently Amended) A method of treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein the at least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent, and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan.
- 2. (Original) The method of claim 1, wherein the indoleamine-2,3-dioxygenase-mediated immunosuppression is meditated by an antigen presenting cell (APC).
- 3. (Currently amended) The method of claim 1, wherein <u>the</u> at least one additional therapeutic agent is an antineoplastic chemotherapy agent <u>previously known to be therapeutically</u> effective for the treatment of said cancer.
- 4. (Currently amended) The method of claim [[3]] 1, wherein the antineoplastic chemotherapeutic agent is select from the group consisting of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, vincristine, ifosfamide, cisplatin, gemcytabine, busulfan, ara-C, and combinations thereof.

Serial No.: 10/780,797 Confirmation No.: 1508 Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2, 3-DIOXYGENASE IN COMBINATION WITH OTHER

THERAPEUTIC MODALITIES

- 5. (Currently amended) [[The]] \underline{A} method of claim 1, treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein at least one additional therapeutic agent is radiation therapy, and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan.
- 6. (Original) The method of claim 5 wherein the radiation therapy is localized radiation therapy delivered to the tumor.
- 7. (Original) The method of claim 5 wherein the radiation therapy is total body irradiation.
- 8. (Cancel)
- 9. (Original) The method of claim 1 wherein the inhibitor of indoleamine-2,3-dioxygenase is 1-methyl-tryptophan.
- 10. (Currently amended) The method of claim [[1]] 5 wherein the inhibitor of indoleamine-2,3-dioxygenase is a D isomer of an inhibitor of indoleamine-2,3-dioxygenase 1-methyl-tryptophan.
- 11. (Currently amended) The method of claim [[10]] 1 wherein the D isomer of an inhibitor

Amendment and Response

Serial No.: 10/780,797 Confirmation No.: 1508 Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2, 3-DIOXYGENASE IN COMBINATION WITH OTHER

THERAPEUTIC MODALITIES

of indoleamine-2,3-dioxygenase is selected from the group <u>consisting</u> of the D isomer of 1-methyl-tryptophan, the D isomer of β -(3-benzofuranyl)-alanine, the D isomer of β -(3-benzo(b)thienyl)-alanine, and the D isomer of 6-nitro-D-tryptophan.

- 12. (Currently amended) The method of claim [[10]] $\underline{5}$ wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of the D isomer of 1-methyl-tryptophan, the D isomer of β -(3-benzo(b)thienyl)-alanine, and the D isomer of 6-nitro-D-tryptophan.
- 13. (Original) The method of claim 1, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.

14-29. (Cancel)

- 30. (Currently amended) The method of claim 1 wherein the additional therapeutic agent is further comprising administering a cytokine.
- 31. (Original) The method of claim 30 wherein the cytokine is granulocyte-macrophage colony stimulating factor (GM-CSF) or flt3-ligand.
- 32. (Withdrawn/currently amended) A method of augmenting the rejection of tumor cells in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the rejection of tumor cells obtained by

Serial No.: 10/780,797 Confirmation No.: 1508 Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2, 3-DIOXYGENASE IN COMBINATION WITH OTHER

THERAPEUTIC MODALITIES

administering both the inhibitor of indoleamine-2,3-dioxygenase and the <u>cytotoxic</u> antineoplastic chemotherapeutic agent is greater than that obtained by administering either the inhibitor of indoleamine-2,3-dioxygenase or the <u>cytotoxic</u> antineoplastic chemotherapeutic agent alone.

- 33. (Currently amended) A method of treating cancer, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the cancer survival rate observed by administering both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is greater than the cancer survival rate observed by administering either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.
- 34. (Withdrawn/currently amended) A method of reducing tumor size or slowing tumor growth in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the tumor size or tumor growth observed with the administration of both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is less than the tumor size or tumor growth observed with the administration of either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.
- 35. (Withdrawn/currently amended) A method augmenting rejection of tumor cells in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzof

Amendment and Response

Serial No.: 10/780,797 Confirmation No.: 1508 Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2, 3-DIOXYGENASE IN COMBINATION WITH OTHER

THERAPEUTIC MODALITIES

benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the rejection of tumor cells wherein the rejection of tumor cells obtained by administering both the inhibitor of indoleamine-2,3-dioxygenase and the radiation therapy is greater than that obtained by administering either the inhibitor of indoleamine-2,3-dioxygenase or the radiation therapy alone.

- 36. (Currently amended) A method of treating cancer, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the cancer survival rate observed by administering both the inhibitor of indoleamine-2,3-dioxygenase and radiation therapy is greater than the cancer survival rate observed by administering either the inhibitor of indoleamine-2,3-dioxygenase or radiation therapy alone.
- 37. (Withdrawn/currently Amended) A method of reducing tumor size or tumor growth in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β -(3-benzofuranyl)-alanine, β -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the tumor size or tumor growth observed with the administration of both the inhibitor of indoleamine-2,3-dioxygenase and radiation therapy is less than the tumor size or tumor growth observed with the administration of either the inhibitor of indoleamine-2,3-dioxygenase or radiation therapy alone.
- 38. (New) The method of claim 5, wherein the indoleamine-2,3-dioxygenase-mediated immunosuppression is meditated by an antigen presenting cell (APC).

Serial No.: 10/780,797 Confirmation No.: 1508 Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2, 3-DIOXYGENASE IN COMBINATION WITH OTHER

THERAPEUTIC MODALITIES

39. (New) The method of claim 5, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.